

The Examiner rejected claims 12-16, 20, and 21 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Office Action at page 2, Item No. 3.

First, the Examiner contended that the term "capable of" in the claims was vague and indefinite. Applicants respectfully traverse this basis for the rejection, since they assert that one skilled in the art would understand what is encompassed by that claim language. The term "capable of" distinguishes the material from other material that does not possess such capability. Solely to expedite prosecution, however, such terms are not included in the newly presented claims. Thus, this basis for the rejection is moot.

Second, the Examiner contends that claims directed to methods of producing TNF inhibitor must include recovery of the inhibitor. Applicants respectfully traverse this basis for the rejection. At the outset, applicants note that the previous method claims did include a harvesting step. Also, applicants disagree that claims directed to producing TNF inhibitor must include a recovery step, since one skilled in the art would understand what is encompassed by claims directed to such processes without the need for a recovery step. In any event, solely to expedite prosecution, the present claims that are directed to methods of producing polypeptides include recovery of the polypeptides.

Third, the Examiner contends that the terms " $\Delta 51$ " and " $\Delta 53$ " are confusing. The Examiner contends that the specification does not adequately define those terms. Applicants respectfully traverse this basis for the rejection. The specification defines

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those terms as used in the present claims. See, e.g., the specification at page 65, lines 15 through 21; and at page 66, lines 5 through 14. Also, solely to expedite prosecution, the newly presented claims define the terms "Δ51" and "Δ53" in view of the amino acid residues of Figure 38.

For all of these reasons, applicants respectfully request reconsideration and withdrawal of the rejection under the second paragraph of section 112.

The Examiner rejected claims 12-21 under 35 U.S.C. § 112, first paragraph, since the specification allegedly enables only nucleic acids encoding full length inhibitor, precursor forms, and certain specific mutants. Office Action at pages 3 to 6, Item No. 4.

The Examiner contends that the claims encompass any nucleic acids encoding TNF inhibitor of unspecified characteristics. Solely to expedite prosecution, all of the presently pending claims define the nucleic acid in the claims in view of particular sequences. Thus, this basis for the rejection is moot.

The Examiner also contends that the fragments or portions encompassed by claims would not be enabled. The Examiner focusses solely on the alleged unpredictability of determining suitable fragments and the specification's failure to provide specific information in advance concerning possible areas of the inhibitors that would be suitable fragments. Specifically, the Examiner contends that "Applicants have not provided teachings, evidence or guidance for the specific residues that can be deleted with **assurance** that they will maintain the desired activity." Office Action at

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page 5 (emphasis added). The Examiner also noted that without further information, one would have to resort to trial and error.

At the outset, applicants respectfully assert that the specification states that the specific fragments "Δ51" and "Δ53" maintained TNF inhibitory activity. See the specification, e.g., at page 69, lines 33 through 34. Also, as discussed above in response to the section 112, second paragraph, rejection, those fragments are defined in the specification.

Moreover, applicants respectfully submit that the Examiner has not sufficiently addressed factors that permit a conclusion of undue experimentation. Specifically, the Examiner fails to consider the routine screening for determining whether the claimed fragments bind to TNF. The Examiner also fails to consider the high level of skill in this art. Applicants submit that the routine screening that one of skill in the art would undertake would not rise to the level of undue experimentation. It would merely require time.

The Examiner cites no authority that would support an enablement rejection based solely on a specification's failure to provide predictable results or "an assurance" of success for all embodiments encompassed by the claims. In fact, the courts have repeatedly held that experimentation is permitted under 35 U.S.C. § 112, first paragraph, even in an unpredictable field. In re Angstadt, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976) (The court stated that to require predictability in advance is contrary to the basic policy of the Patent Act).

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The burden is on the Examiner to establish a *prima facie* case that undue experimentation would be required to make and use the claimed invention. Id. Here the Examiner has not considered the routine screening that one skilled in the art could carry out. The Examiner concludes that undue experimentation would be required, but provides no evidence concerning the type of experimentation involved or any particular difficulties one skilled in the art would encounter in screening the claimed fragments for their ability to bind to TNF.

Unpredictability in advance, however, does not establish undue experimentation, since routine screening can be employed to test for binding activity of the claimed fragments. Fragments that bind to TNF are within the claims, and those that do not bind to TNF are not covered by the claims. Even if not predictable in advance, such routine screening renders the present claims enabled in view of the present specification. Thus, applicants traverse this basis for the rejection.

For all of these reasons, applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under the first paragraph of section 112.

The Examiner provisionally rejected claims 12-21 under the judicially created doctrine of obviousness-type double patenting over claims of U.S. Patent Application Serial No. 08/092,538. Office Action at page 6, Item No. 5. Without addressing the substantive merits of this rejection, applicants note that Serial No. 08/092,538 recently was abandoned. Thus, this provisional rejection is moot.

The Examiner rejected claims 12-21 "under 35 U.S.C. § 102(a) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Wallach [European Patent Application No. 0 308 378]." Office Action at page 7, Item No. 6. The Examiner contends that Wallach "discloses DNA sequences that will encode for a protein, although referred to by a different name, that is considered a binding protein for TNF; as well as the recombinant production of such (see the claims and examples)." *Id.* The Examiner then notes that the protein of Wallach has the same N-terminal sequence of a sequence of the present application, and contends that it appears to be the same protein. The Examiner also contends that the " $\Delta$ 51" and " $\Delta$ 53" forms of the protein would have been obvious since Wallach discusses the possibility of modifying the protein. Applicants respectfully traverse this rejection.

As asserted during the interview, Wallach failed to show the presently claimed DNA. Wallach discusses the possibility of obtaining DNA, but provides no actual disclosure of the structure of such DNA. Thus, under proper law, Wallach cannot anticipate nor can it render obvious the presently pending claims, which are directed to particular nucleic acids, vectors containing nucleic acids, host cells containing particular nucleic acids, and methods of producing polypeptides and recombinant host cells using particular nucleic acids.

Specifically, in *In re Deuel*, the Federal Circuit held that knowledge of a protein, even if it is partially sequenced, does not render obvious the DNA that encodes that protein, even if methods had been known to isolate DNA using amino acid sequence

information. In re Deuel, 34 U.S.P.Q.2d 1210, 1215-16 (Fed. Cir. 1995). In that case, the prior art included a partial amino acid sequence and general cloning methods that allegedly could have been used to obtain the claimed DNA using the partial amino acid sequence information.

The Federal Circuit stated that "[t]he PTO's focus on known methods of potentially isolating the claimed DNA molecule is also misplaced because the claims at issue define compounds, not methods." Id. at 1215. The Court also stated that "a conceived method of preparing some undefined DNA does not define it with the precision necessary to render it obvious over the protein it encodes." Id. at 1216. Additionally, the Court held that a claim encompassing degenerate DNA sequences encoding a particular protein would not have been obvious in view of a disclosure of a partial amino acid sequence of that protein and a disclosure of methods of using partial amino acid sequence information to obtain other DNA. Id.

In summary, the Court held that unless the structure of the DNA was disclosed, proposed methods of obtaining the DNA would not render obvious the claimed DNA. Since Wallach would have failed to show DNA structure, it could not have rendered obvious the present claims. Applicants do not acquiesce in the Examiner's statements concerning the identity of the protein and the " $\Delta 51$ " and " $\Delta 53$ " forms, but do not address such statements, since the absence of DNA structure in Wallach alone renders the rejection unsupportable.

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For these reasons, applicants respectfully traverse the section 102 and section 103 rejections over Wallach and request reconsideration and withdrawal of them.

Also during the interview, copending applications of Hauptmann et al. and applications of Brewer et al. were discussed. Presently, the following Hauptmann et al. applications are pending: U.S. Serial Nos. 08/383,676; 08/477,638; 08/477,639; 08/484,312, and 08/484,307. Also the following additional Brewer et al. applications are pending: U.S. Serial Nos. 08/848,292; 08/375,242; and 08/485,439 (this last application was abandoned and petition to revive has been filed). (Brewer et al.'s U.S. Application Serial No. 08/092,538 recently was abandoned.) The present application and all of the Hauptmann et al. applications listed above and the Brewer et al. applications listed above are presently assigned to Synergen, Inc. It is the understanding of Paul Barker that the Hauptmann et al. applications were not assigned to Synergen, Inc. at the time of the invention in the Hauptmann et al. applications.

When Serial Nos. 08/477,638, 08/477,639, 08/484,307 and 08/484,312 were filed, the Rule 60 forms of each application erroneously indicated that the parent application (U.S. Serial No. 08/383,676) had been assigned to Amgen Acquisitions Subsidiary, Inc. The parent application in fact was assigned to Synergen, Inc., and thus the continuation or divisional applications are also assigned to Synergen, Inc. Synergen, Inc. has become a subsidiary of Amgen Inc. The Brewer et al. applications, the present application, and the Hauptmann et al. applications still are assigned to Synergen, Inc. Synergen, Inc.'s name has been changed to Amgen Boulder Inc., and

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that name change has not yet been recorded at the U.S. Patent and Trademark Office. As discussed at the interview, applicants intend to pursue separately patentable subject matter in the Hauptmann et al. applications on the one hand and the Brewer et al. applications on the other hand.

Applicants request that Examiner Draper call the undersigned at (202) 408-4067 if she believes that a discussion would further advance prosecution of this case.

Applicants submit that all of the pending and presently considered claims are in condition for allowance. Thus, applicants respectfully request issuance of a Notice of Allowance.

If there are any fees due in connection with the filing of Preliminary Amendment, please charge the fees to our Deposit Account No. 06-0916. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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By:



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